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<p>(54) Title: METHODS FOR REGULATING SKIN APPEARANCE</p> <p>(57) Abstract</p> <p>The present invention relates to methods for preventing or treating skin disorders using flavonoid compounds. The present invention also relates to methods for regulating skin condition.</p>			

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## METHODS FOR REGULATING SKIN APPEARANCE

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### TECHNICAL FIELD

The present invention relates to methods for preventing or treating skin disorders using flavonoid compounds. The present invention also relates to methods for regulating skin condition.

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### CROSS REFERENCE

This application claims priority under Title 35, United States Code 119(e) from Provisional Application Serial No. 60/078,148, filed March 16, 1998

### BACKGROUND OF THE INVENTION

Many personal care products currently available to consumers are directed 15 primarily to improving the health and/or physical appearance of the skin. Among these skin care products, many are directed to delaying, minimizing or even eliminating skin wrinkling and other histological changes typically associated with the aging of skin or environmental damage to human skin. Other types of products are useful for imparting moisturization to dry skin, providing photoprotection for skin 20 exposed to sunlight, and bringing about desired control of pigmentation, especially lightening of darkened or hyperpigmented skin.

Skin is subject to insults by many extrinsic and intrinsic factors. Extrinsic factors include ultraviolet radiation (e.g., from sun exposure), environmental pollution, wind, heat or infrared radiation (IR), low humidity, harsh surfactants, 25 abrasives, and the like. Intrinsic factors include chronological aging and other biochemical changes from within the skin. Whether extrinsic or intrinsic, these factors result in visible signs of skin aging and environmental damage, such as wrinkling and other forms of roughness (including increased pore size, flaking and skin lines), and other histological changes associated with skin aging or damage. To 30 many people, skin wrinkles are a reminder of the disappearance of youth. As a result, the elimination of wrinkles has become a booming business in youth-conscious

societies. Treatments range from cosmetic creams and moisturizers to various forms of cosmetic surgery.

Extrinsic or intrinsic factors may result in the thinning and general  
35 degradation of the skin. For example, as the skin naturally ages, there is a reduction in the cells and blood vessels that supply the skin. There is also a flattening of the dermal-epidermal junction which results in weaker mechanical resistance of this junction. See, for example, Oikarinen, "The Aging of Skin: Chronoaging Versus Photoaging," *Photodermatol. Photoimmunol. Photomed.*, vol. 7, pp. 3-4, 1990,  
40 which is incorporated by reference herein in its entirety.

It has now been found that topical compositions containing select flavonoid compounds provide benefits in regulating skin condition previously unrecognized in the art of which the present inventor is aware. For example, such compositions regulate the signs of skin aging, especially visible and/or tactile discontinuities in skin  
45 texture associated with aged skin, including fine lines and wrinkles.

It is therefore an object of the present invention to provide methods for prophylactically and/or therapeutically regulating mammalian skin condition (especially of human skin, more especially human facial and body skin), using topical compositions containing flavonoid compounds.

50 It is another object of the present invention to provide methods for prophylactically and/or therapeutically regulating signs of mammalian skin aging using topical compositions containing flavonoid compounds.

55 It is another object of the present invention to provide methods for prophylactically and/or therapeutically regulating visible and/or tactile discontinuities in mammalian skin texture, including fine lines, wrinkles, enlarged pores, roughness, dryness and other skin texture discontinuities associated with aged skin, using topical compositions containing flavonoid compounds.

These and other objects of this invention will become apparent in light of the following disclosure.

60 SUMMARY OF THE INVENTION

The present invention relates to methods for regulating the visible and/or tactile discontinuities or abnormalities in mammalian skin, comprising applying to

skin in need of such treatment a safe and effective amount of a skin care composition comprising:

- 65       (a) a safe and effective amount of an agent for regulating such visible and/or tactile discontinuities or abnormalities consisting essentially of flavonoids selected from the group consisting of:
- (i) flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof;
- 70       (ii) chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof;
- (iii) flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof;
- 75       (iv) one or more isoflavones;
- (v) coumarins selected form the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof;
- 80       (vi) chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures thereof;
- (vii) one or more dicoumarols;
- (viii) one or more chromanones;
- 85       (ix) one or more chromanols; and
- (x) mixtures thereof;

and

- 90       (b) a dermatologically acceptable carrier for the regulating agent.

**DETAILED DESCRIPTION OF THE INVENTION**

All percentages and ratios used herein are by weight of the total composition and all measurements made are at 25°C, unless otherwise designated.

95        The compositions of the present invention can comprise, consist essentially of, or consist of, the essential as well as optional ingredients and components described herein. As used herein, "consisting essentially of" means that the composition or component may include additional ingredients, but only if the additional ingredients do not materially alter the basic and novel characteristics of the claimed compositions or methods.

100      All publications cited herein are hereby incorporated by reference in their entirety.

      The term "topical application", as used herein, means to apply or spread the compositions of the present invention onto the surface of the skin.

105      The term "dermatologically-acceptable," as used herein, means that the compositions or components thereof so described are suitable for use in contact with human skin without undue toxicity, incompatibility, instability, allergic response, and the like.

110      The term "safe and effective amount" as used herein means an amount of a compound or composition sufficient to significantly induce a positive benefit, preferably a positive skin appearance or feel benefit, including independently the benefits disclosed herein, but low enough to avoid serious side effects, i.e., to provide a reasonable benefit to risk ratio, within the scope of sound judgment of the skilled artisan.

115      The compositions of the present invention are useful for topical application and for regulating skin condition, including visible and/or tactile discontinuities in skin (especially the skin surface; such discontinuities are generally undesired). Such discontinuities may be induced or caused by internal and/or external factors, and include the signs of skin aging described herein. "Regulating skin condition" includes prophylactically regulating and/or therapeutically regulating skin condition, including visible and/or tactile discontinuities in skin such as, but not limited to, regulating 120 visible and/or tactile discontinuities in the texture of skin, reducing post-inflammatory hyperpigmentation, regulating non-melanin discoloration of skin, regulating moisturization and barrier properties of skin, regulating epidermal differentiation of skin, regulating exfoliation of skin, thickening of skin to reduce skin atrophy,

regulating the elasticity of skin, reducing oily skin, regulating cellulite in skin,  
125 regulating pruritus in skin, and promoting wound healing in skin. As used herein,  
prophylactically regulating skin condition includes delaying, minimizing and/or  
preventing visible and/or tactile discontinuities in skin. As used herein,  
therapeutically regulating skin condition includes ameliorating, e.g., diminishing,  
minimizing and/or effacing, discontinuities in skin. Regulating skin condition  
130 involves improving skin appearance and/or feel.

The compositions of the present invention are useful for regulating signs of  
skin aging, more especially visible and/or tactile discontinuities in skin texture  
associated with aging. "Regulating the signs of skin aging" includes prophylactically  
regulating and/or therapeutically regulating one or more of such signs (similarly,  
135 regulating a given sign of skin aging, e.g., lines, wrinkles or pores, includes  
prophylactically regulating and/or therapeutically regulating that sign). As used  
herein, prophylactically regulating such signs includes delaying, minimizing and/or  
preventing signs of skin aging. As used herein, therapeutically regulating such signs  
includes ameliorating, e.g., diminishing, minimizing and/or effacing signs of skin  
140 aging.

"Signs of skin aging" include, but are not limited to, all outward visibly and  
tactilely perceptible manifestations as well as any other macro or micro effects due to  
skin aging. Such signs may be induced or caused by intrinsic factors or extrinsic  
factors, e.g., chronological aging and/or environmental damage (e.g., sunlight, UV,  
145 smoke, ozone, pollutants, stress, etc.). These signs may result from processes which  
include, but are not limited to, the development of textural discontinuities such as  
wrinkles, including both fine superficial wrinkles and coarse deep wrinkles, skin lines,  
facial frown lines, expression lines, rhytides, dermatoheliosis, photodamage,  
premature skin aging, crevices, bumps, pits, large pores (e.g., associated with adnexal  
150 structures such as sweat gland ducts, sebaceous glands, or hair follicles),  
"orange'peel" skin appearance, dryness, scaliness, flakiness and/or other forms of  
skin unevenness or roughness; blemishes such as acne, pimples, breakouts; excess  
skin oil problems such as over production of sebum, oiliness, facial shine, foundation  
breakthrough; abnormal desquamation (or exfoliation) or abnormal epidermal

155 differentiation (e.g., abnormal skin turnover) such as scaliness, flakiness, keratoses, hyperkeratinization; inadequate skin moisturization (or hydration) such as caused by skin barrier damage, environmental dryness; loss of skin elasticity (loss and/or inactivation of functional skin elastin) such as elastosis, sagging (including puffiness in the eye area and jowls), loss of skin firmness, loss of skin tightness, loss of skin  
160 recoil from deformation; non-melanin skin discoloration such as undereye circles, blotching (e.g., uneven red coloration due to, e.g., rosacea), sallowness (pale color), discoloration caused by telangiectasia or spider vessels; melanin-related hyperpigmented (or unevenly pigmented) skin regions such as age spots (liver spots, brown spots) and freckles; post-inflammatory hyperpigmentation such as that which occurs following an inflammatory event (e.g., as an acne lesion, in-grown hair, insect/spider bite or sting, scratch, cut, wound, abrasion, and the like); atrophy such as, but not limited to, that associated with aging or steroid use; other histological or microscopic alterations in skin components such as ground substance (e.g., hyaluronic acid, glycosaminoglycans, etc.), collagen breakdown and structural  
165 alterations or abnormalities (e.g., changes in the stratum corneum, dermis, epidermis, the skin vascular system such as telangiectasia or spider vessels); tissue responses to insult such as itch or pruritus; and alterations to underlying tissues (e.g., subcutaneous fat, cellulite, muscles, trabeculae, septae, and the like), especially those proximate to the skin.

175 It is to be understood that the present invention is not to be limited to regulation of the above mentioned "signs of skin aging" which arise due to mechanisms associated with skin aging, but is intended to include regulation of said signs irrespective of the mechanism of origin. As used herein, "regulating skin condition" is intended to include regulation of such signs irrespective of the mechanism of origin.

180 The present invention is especially useful for therapeutically regulating visible and/or tactile discontinuities in mammalian skin texture, including texture discontinuities associated with skin aging. As used herein, therapeutically regulating such discontinuities includes ameliorating, e.g., diminishing, minimizing and/or effacing visible and/or tactile discontinuities in the texture of mammalian skin, to

thereby provide improved skin appearance and/or feel, e.g., a smoother, more even appearance and/or feel. Such visible and/or tactile discontinuities in skin texture include crevices, bumps, pores, fine lines, wrinkles, scales, flakes and/or other forms of textural unevenness or roughness associated with skin aging. For example, the  
190 length, depth, and/or other dimension of lines and/or wrinkles are decreased, the apparent diameter of pores decreases, or the apparent height of tissue immediately proximate to pore openings approaches that of the interadnexal skin.

The present invention is also especially useful for prophylactically regulating visible and/or tactile discontinuities in mammalian skin texture, including texture discontinuities associated with skin aging. As used herein, prophylactically regulating such discontinuities includes delaying, minimizing and/or preventing visible and/or tactile discontinuities in the texture of mammalian skin, to thereby provide improved skin appearance and/or feel, e.g., a smoother, more even appearance and/or feel.  
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200 The compositions of the present invention, including the essential and optional components thereof, are described in detail hereinafter.

#### ESSENTIAL COMPONENTS

##### Flavonoid compounds

205 An essential of the compositions of the present invention is a flavonoid compound. Flavonoids are broadly disclosed in U.S. Patents 5,686,082 and 5,686,367, both of which are herein incorporated by reference. Flavonoids suitable for use in the present invention are flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof; chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof; flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof; one or more isoflavones; coumarins selected from the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof; chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures  
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thereof; one or more dicoumarols; one or more chromanones; one or more chromanols; isomers (e.g., cis/trans isomers) thereof; and mixtures thereof. By the  
220 term "substituted" as used herein means flavonoids wherein one or more hydrogen atom of the flavonoid has been independently replaced with hydroxyl, C1-C8 alkyl, C1-C4 alkoxy, O-glycoside, and the like or a mixture of these substituents.

Examples of suitable flavonoids include, but are not limited to, unsubstituted  
flavanone, mono-hydroxy flavanones (e.g., 2'-hydroxy flavanone, 6-hydroxy  
225 flavanone, 7-hydroxy flavanone, etc.), mono-alkoxy flavanones (e.g., 5-methoxy  
flavanone, 6-methoxy flavanone, 7-methoxy flavanone, 4'-methoxy flavanone, etc.),  
unsubstituted chalcone (especially unsubstituted trans-chalcone), mono-hydroxy  
chalcones (e.g., 2'-hydroxy chalcone, 4'-hydroxy chalcone, etc.), di-hydroxy  
chalcones (e.g., 2',4-dihydroxy chalcone, 2',4'-dihydroxy chalcone, 2,2'-dihydroxy  
230 chalcone, 2',3-dihydroxy chalcone, 2',5'-dihydroxy chalcone, etc.), and tri-hydroxy  
chalcones (e.g., 2',3',4'-trihydroxy chalcone, 4,2',4'-trihydroxy chalcone, 2,2',4'-  
trihydroxy chalcone, etc.), unsubstituted flavone, 7,2'-dihydroxy flavone, 3',4'-  
dihydroxy naphthoflavone, 4'-hydroxy flavone, 5,6-benzoflavone, and 7,8-  
benzoflavone, unsubstituted isoflavone, daidzein (7,4'-dihydroxy isoflavone), 5,7-  
235 dihydroxy-4'-methoxy isoflavone, soy isoflavones (a mixture extracted from soy),  
unsubstituted coumarin, 4-hydroxy coumarin, 7-hydroxy coumarin, 6-hydroxy-4-  
methyl coumarin, unsubstituted chromone, 3-formyl chromone, 3-formyl-6-isopropyl  
chromone, unsubstituted dicoumarol, unsubstituted chromanone, unsubstituted  
chromanol, and mixtures thereof..

240 Preferred for use herein are unsubstituted flavanone, methoxy flavanones,  
unsubstituted chalcone, 2',4-dihydroxy chalcone, and mixtures thereof. Most  
preferred are unsubstituted flavanone, unsubstituted chalcone (especially the trans  
isomer), and mixtures thereof.

They can be synthetic materials or obtained as extracts from natural sources  
245 (e.g., plants). The naturally sourced material can also further be derivatized (e.g., an  
ester or ether derivative prepared following extraction from a natural source).  
Flavonoid compounds useful herein are commercially available from a number of  
sources, e.g., Indofine Chemical Company, Inc. (Somerville, New Jersey), Steraloids,

Inc. (Wilton, New Hampshire), and Aldrich Chemical Company, Inc. (Milwaukee, 250 Wisconsin).

Mixtures of the above flavonoid compounds may also be used.

The herein described flavonoid compounds are preferably present in the instant invention at concentrations of from about 0.01% to about 20%, more preferably from about 0.1% to about 10%, and most preferably from about 0.5% to 255 about 5%.

Carrier

Another essential ingredient of the present invention is a dermatologically acceptable carrier. The phrase "dermatologically -acceptable carrier", as used herein, means that the carrier is suitable for topical application to the skin, has good aesthetic 260 properties, is compatible with the actives of the present invention and any other components, and will not cause any untoward safety or toxicity concerns. A safe and effective amount of carrier is from about 50% to about 99.99%, preferably from about 99.9% to about 80%, more preferably from about 98% to about 90%, most preferably from about 95% to about 90% of the composition.

265 The carrier can be in a wide variety of forms. For example, emulsion carriers, including, but not limited to, oil-in-water, water-in-oil, water-in-oil-in-water, and oil-in-water-in-silicone emulsions, are useful herein. These emulsions can cover a broad range of viscosities, e.g., from about 100 cps to about 200,000 cps. These emulsions can also be delivered in the form of sprays using either mechanical pump containers 270 or pressurized aerosol containers using conventional propellants. These carriers can also be delivered in the form of a mousse. Other suitable topical carriers include anhydrous liquid solvents such as oils, alcohols, and silicones (e.g., mineral oil, ethanol, isopropanol, dimethicone, cyclomethicone, and the like); aqueous-based single phase liquid solvents (e.g., hydro-alcoholic solvent systems); and thickened versions of 275 these anhydrous and aqueous-based single phase solvents (e.g., where the viscosity of the solvent has been increased to form a solid or semi-solid by the addition of appropriate gums, resins, waxes, polymers, salts, and the like). Examples of topical carrier systems useful in the present invention are described in the following four references all of which are incorporated herein by reference in their entirety: "Sun

280 Products Formulary" Cosmetics & Toiletries, vol. 105, pp. 122-139 (December 1990); "Sun Products Formulary", Cosmetics & Toiletries, vol. 102, pp. 117-136 (March 1987); U.S. Patent No. 4,960,764 to Figueroa et al., issued October 2, 1990; and U.S. Patent No. 4,254,105 to Fukuda et al., issued March 3, 1981.

285 The carriers of the present invention can comprise from about 50% to about 99% by weight of the compositions of the present invention, preferably from about 75% to about 99%, and most preferably from about 85% to about 95%.

290 Preferred cosmetically and/or pharmaceutically acceptable topical carriers include hydro-alcoholic systems and oil-in-water emulsions. When the carrier is a hydro-alcoholic system, the carrier can comprise from about 0% to about 99% of ethanol, isopropanol, or mixtures thereof, and from about 1% to about 99% of water. More preferred is a carrier comprising from about 5% to about 60% of ethanol, isopropanol, or mixtures thereof, and from about 40% to about 95% of water. Especially preferred is a carrier comprising from about 20% to about 50% of ethanol, isopropanol, or mixtures thereof, and from about 50% to about 80% of water. When 295 the carrier is an oil-in-water emulsion, the carrier can include any of the common excipient ingredients for preparing these emulsions. A more detailed discussion of suitable carriers is found in U.S. Patent 5,605,894 to Blank et al., and, U.S. Patent 5,681,852 to Bissett, both of which are herein incorporated by reference in their entirety.

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#### OPTIONAL COMPONENTS

The skin regulating compositions of the present invention may optionally comprise additional skin actives. Non-limiting examples of such skin actives include vitamin B3 compounds such as those described in PCT application WO 97/39733, published October 30, 1997, to Oblong et al., herein incorporated by reference in its 305 entirety; hydroxy acids such as salicylic acid; exfoliation or desquamatory agents such as zwitterionic surfactants; sunscreens such as 2-ethylhexyl-p-methoxycinnamate, 4,4'-*t*-butyl methoxydibenzoyl-methane, octocrylene, phenyl benzimidazole sulfonic acid; sun-blocks such as zinc oxide and titanium dioxide; anti-inflammatory agents; anti-oxidants/radical scavengers such as tocopherol and esters thereof; metal chelators, especially iron chelators; retinoids such as retinol, retinyl palmitate, retinyl

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acetate, retinyl propionate, and retinal; N-acetyl-L-cysteine and derivatives thereof; hydroxy acids such as glycolic acid; keto acids such as pyruvic acid; benzofuran derivatives; depilatory agents (e.g., sulfhydryl compounds); skin lightening agents (e.g., arbutin, kojic acid, hydroquinone, ascorbic acid and derivatives such as ascorbyl phosphate salts, placental extract, and the like); anti-cellulite agents (e.g., caffeine, theophylline); moisturizing agents; anti-microbial agents; anti-androgens; and skin protectants. Mixtures of any of the above mentioned skin actives may also be used. A more detailed description of these actives is found in U.S. Patent 5,605,894 to Blank et al. (previously incorporated by reference). Preferred skin actives include hydroxy acids such as salicylic acid, sunscreen, antioxidants and mixtures thereof.

Other conventional skin care product additives may also be included in the compositions of the present invention. For example, urea, guanidine, glycerol, petrolatum, mineral oil, sugar esters and polyesters, polyolefins, methyl isostearate, ethyl isostearate, cetyl ricinoleate, isononyl isononanoate, isoheptadecane, lanolin, lanolin esters, cholesterol, pyrrolidone carboxylic acid/salt (PCA), trimethyl glycine (betaine), tranexamic acid, amino acids (e.g., serine, alanine, threonine, histidine) and/or their salts, panthenol and its derivatives, collagen, hyaluronic acid, elastin, hydrolysates, primrose oil, jojoba oil, epidermal growth factor, soybean saponins, mucopolysaccharides, and mixtures thereof may be used. Other suitable additives or skin actives are discussed in further detail in PCT application WO 97/39733, published October 30, 1997, to Oblong et al., previously incorporated by reference in its entirety.

#### Preparation of Compositions

The compositions of the present invention are generally prepared by conventional methods such as are known in the art of making topical compositions. Such methods typically involve mixing of the ingredients in one or more steps to a relatively uniform state, with or without heating, cooling, application of vacuum, and the like.

#### Methods for Regulating Skin Condition

The compositions of the present invention are useful for regulating mammalian skin condition (especially human skin, more especially human facial skin),

including visible and/or tactile discontinuities in skin, signs of skin aging, and visible and/or tactile discontinuities in skin associated with skin aging (including fine lines, wrinkles, large pores, surface roughness, dryness and other texture discontinuities 345 associated with aged skin). Such regulation includes prophylactic and therapeutic regulation.

Regulating skin condition involves topically applying to the skin a safe and effective amount of a composition of the present invention. The amount of the composition which is applied, the frequency of application and the period of use will 350 vary widely depending upon the level of the flavonoid compound and/or other components of a given composition and the level of regulation desired, e.g., in light of the level of skin aging present in the subject and the rate of further skin aging.

In a preferred embodiment, the composition is chronically applied to the skin. By "chronic topical application" is meant continued topical application of the 355 composition over an extended period during the subject's lifetime, preferably for a period of at least about one week, more preferably for a period of at least about one month, even more preferably for at least about three months, even more preferably for at least about six months, and more preferably still for at least about one year. While benefits are obtainable after various maximum periods of use (e.g., five, ten or 360 twenty years), it is preferred that chronic application continue throughout the subject's lifetime. Typically applications would be on the order of about once per day over such extended periods, however application rates can vary from about once per week up to about three times per day or more.

A wide range of quantities of the compositions of the present invention can be 365 employed to provide a skin appearance and/or feel benefit. Quantities of the present compositions which are typically applied per application are, in mg composition/cm<sup>2</sup> skin, from about 0.1 mg/cm<sup>2</sup> to about 10 mg/cm<sup>2</sup>. A particularly useful application amount is about 2 mg/cm<sup>2</sup>.

Regulating skin condition is preferably practiced by applying a composition in 370 the form of a skin lotion, cream, gel, emulsion, spray, conditioner, cosmetic, lipstick, foundation, nail polish, or the like which is intended to be left on the skin for some esthetic, prophylactic, therapeutic or other benefit (i.e., a "leave-on" composition).

After applying the composition to the skin, it is preferably left on the skin for a period of at least about 15 minutes, more preferably at least about 30 minutes, even more preferably at least about 1 hour, most preferably for at least several hours, e.g., up to about 12 hours. Any part of the external portion of the face, hair, and/or nails can be treated, e.g., face, lips, under-eye area, eyelids, scalp, neck, torso, arms, hands, legs, fingernails, toenails, scalp hair, eyelashes, eyebrows, etc.

Another approach to ensure a continuous exposure of the skin to at least a minimum level of the flavonoid compound is to apply the compound by use of a patch applied, e.g., to the face. Such an approach is particularly useful for problem skin areas needing more intensive treatment. The patch can be occlusive, semi-occlusive or non-occlusive. The flavonoid compound composition can be contained within the patch or be applied to the skin prior to application of the patch. The patch can also include additional actives such as chemical initiators for exothermic reactions such as those described in PCT application WO 9701313 to Burkett et al. The patch is preferably left on the skin for a period of at least about 15 minutes, more preferably at least about 30 minutes, even more preferably at least about 1 hour, most preferably at night as a form of night therapy.

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#### EXAMPLES

The following examples further describe and demonstrate embodiments within the scope of the present invention. The examples are given solely for the purpose of illustration and are not to be construed as limitations of the present invention, as many variations thereof are possible without departing from the spirit and scope of the invention.

##### Example 1

A skin cream is prepared by conventional methods from the following components.

	Ingredient (CTFA Name)	Weight %
PHASE A:	Water U.S.P.	55.31
	Disodium EDTA	0.13
	Methyl Paraben	0.25
	Glycerin	3.00
	2',4-dihydroxy chalcone	2.00

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	Zinc Citrate	1.00
PHASE B:	Cetyl Alcohol	0.56
	Stearyl Alcohol	2.03
	Behenyl Alcohol	0.22
	Steareth-21 (Brij 721)	0.37
	Steareth-2 (Brij 72)	1.10
	Distearyldimonium chloride (Varisoft TA-100)	0.95
	Propyl Paraben	0.10
	Polypropylene glycol-15 stearyl ether (Arlamol E)	3.25
PHASE C:	Polypropylene glycol-15 stearyl ether (Arlamol E)	2.17
	titanium dioxide	0.75
PHASE D:	Citric acid	0.19
	water U.S.P.	22.00
	50% NaOH	0.94
PHASE E:	Benzyl Alcohol	0.50
	Silicone fluid (DC Q2 - 1401; cyclomethicone/dimethiconol - 50/50 blend	0.75
	dimethicone 10 cst	1.00
	polyethylene Low Density Beads	1.00
PHASE F:	Fragrance	0.10
PHASE G:	50% NaOH	0.33

Blend the A phase components with a suitable mixer (e.g., Tekmar model RW20DZM), heating while stirring to a temperature of 70-80°C. Separately, blend the B phase components with a suitable mixer and heat with mixing to melt the components. Separately, blend the C phase components and mill to obtain an acceptably smooth mixture (e.g., using a Tekmar T50 Mill).

405 Add the C phase mixture to the B phase mixture and mix. Then add the resulting mix to the A phase mixture with mixing, cool with a cold water bath and mill, then continue stirring. Remove the combination from the bath, with continued stirring, once the temperature reaches 40°C.

Separately, blend the D phase components by stirring until dissolved, then add this to the combination of A-C materials.

410 Separately, blend the E phase components by mixing until smooth and continuous, then add this to the combination of the A-D materials. Add and mix the fragrance, then the NaOH. Adjust the pH as necessary to 5.5.

415 Apply the composition to a subject's wrinkled, aged, or photodamaged facial skin at the rate of 2 mg composition/cm<sup>2</sup> skin once or twice daily for a period of at least 3-6 months to reduce fine lines and wrinkles and improve skin surface texture.

Alternatively, the 2',4-dihydroxy chalcone can be replaced with an equivalent quantity of another flavonoid (e.g., another chalcone, flavanone, isoflavone, coumarin, flavone, chromone, dicoumarol, chromanone, chromanol, or mixtures thereof).

420 Example 2

An emulsion is prepared by conventional methods from the following components:

Ingredient	Weight %
Silicone fluid (Dow Corning DC 345)	15.0
Silicone fluid (Dow Corning DC 3225C)	2.5
Silicone fluid (Goldschmidt Abil We09)	2.5
Water	71.4
Unsubstituted flavanone	5.0
Tetrasodium EDTA	0.1
Benzyl alcohol	0.3
Methyl paraben	0.2
Glycerin	3.0

425 Form the water phase in a suitable vessel charged with the water as follows: add the glycerin to the water with stirring. Add to this mixture with stirring the methyl paraben dissolved in the benzyl alcohol. Add to this mixture with stirring the EDTA.

Form the silicone phase in a separate suitable vessel by adding and stirring together the silicone fluids and the unsubstituted flavanone.

Add the water phase to the silicone phase slowly with stirring to form the  
430 emulsion.

Apply the resulting composition to a subject's wrinkled, aged, or photodamaged facial skin at the rate of 2 mg composition/cm<sup>2</sup> skin once or twice daily for a period of at least 3-6 months to reduce fine lines and wrinkles and improve skin surface texture.

435 Alternatively, the unsubstituted flavanone can be replaced with an equivalent quantity of another flavonoid (e.g., chalcone, another flavanone, isoflavone, coumarin, flavone, chromone, dicoumarol, chromanone, chromanol, or mixtures thereof).

440

### Example 3

A skin cream is prepared by conventional methods from the following components.

	Ingredient (CTFA Name)	Weight %
PHASE A:	Water U.S.P.	61.96
	Disodium EDTA	0.15
	Glycerin	5
	2'-hydroxy flavanone	2.0
PHASE B:	Cetyl hydroxy ethyl cellulose	0.15
	Methyl Paraben	0.25
PHASE C:	Cetyl Alcohol	0.5
	Stearyl Alcohol	0.5
	Behenyl Alcohol	0.5
	Cetyl ricinoleate	3
	Steareth-2 (Brij 72)	1.05
	Distearyldimonium chloride (Varisoft TA-100)	0.25
	Propyl Paraben	0.10

	Myristyl myristate	1.5
	Caprylic/Caprylyglycerides	1.5
	Mineral oil	2
	Fatty acid ester of sugar*	1
	Polypropylene glycol-15 stearyl ether (Arlamol E)	1.05
PHASE D:	dimethicone 10 cst (Dow Corning)	2
PHASE E:	Water U.S.P.	15
PHASE F:	Benzyl Alcohol	0.5
PHASE G:	50% NaOH	0.04

\* A C1-C30 monoester or polyester of sugars and one or more carboxylic acid moieties as described herein, preferably a sucrose polyester in which the degree of esterification is 7-8, and in which the fatty acid moieties are C18 mono- and/or di-unsaturated and behenic, in a molar ratio of unsaturates:behenic of 1:7 to 3:5, more preferably the octaester of sucrose in which there are about 7 behenic fatty acid moieties and about 1 oleic acid moiety in the molecule, e.g., sucrose ester of cottonseed oil fatty acids.

445 450 Blend the A phase components with a suitable mixer (e.g., Tekmar model RW20DZM), heating while stirring to a temperature of about 70-80°C. Add the cetyl hydroxy ethyl cellulose and methyl paraben with mixing at about 70-80°C to melt the components. Separately, blend the C phase components and mill to obtain an acceptably smooth mixture (e.g., using a Tekmar T50 Mill).

455 460 Add the C phase mixture to the above mixture and mix. Remove the combination from the bath, with continued stirring, once the temperature reaches about 45°C. Add the dimethicone and mix.

460 Separately, blend the E phase components by mixing until smooth and continuous, then add this to the above mixture. Add and mix in the benzyl alcohol, then the NaOH. Adjust the pH as necessary to 7.

460 Apply the composition to a subject's wrinkled, aged, or photodamaged facial skin at the rate of 2 mg composition/cm<sup>2</sup> skin once or twice daily for a period of at least 3-6 months to reduce fine lines and wrinkles and improve skin surface texture.

465 Alternatively, the 2'-hydroxy flavanone can be replaced with an equivalent quantity of another flavonoid (e.g., chalcone, another flavanone, isoflavone, coumarin, flavone, chromone, dicoumarol, chromanone, chromanol, or mixtures thereof).

#### Example 4

470 A skin cream is prepared by conventional methods from the following components.

	Component	Weight %
PHASE A:	benzyl alcohol	0.30
	methyl p-hydroxybenzoate (a.k.a. methylparaben)	0.20
	ethanol	3.00
PHASE B:	water	60.60-61.35
	disodium EDTA	0.50
	glycerol	10.00
	hexylene glycol	2.00
	triethanol amine	0.05
	butylated hydroxytoluene	0.10
PHASE C:	Dow Corning 345 Fluid	12.50
	Abil WE-09	2.50
	Dow Corning -3225C	2.50
	petrolatum	1.50
	unsubstituted chalcone	2.00
	retinol (10% in soybean oil)	0.75-1.50
	fatty acid ester of sugar*	1.00

\* See Example 3

475 Blend the A phase components with a suitable mixer (e.g., Tekmar model RW20DZM). Blend the B phase components into the A phase with a suitable mixer. Separately, blend the C phase components until they are uniform. Add the C phase mixture to the A/B phase mixture, mix until uniform and emulsified, and then mill to obtain an acceptably smooth mixture (e.g., using a Tekmar T50 Mill).

480 Apply the composition to a subject's wrinkled, intrinsically aged, or photodamaged facial skin at the rate of 2 mg composition/cm<sup>2</sup> skin once or twice daily for a period of at least 3-6 months to improve skin surface texture, including diminishing fine lines and wrinkles.

An alternative skin cream having reduced retinol levels can be prepared in the same manner from the above components wherein the retinol is added in an amount

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485 of 0.025% (0.25% of 10% retinol in soybean oil), quo sine to 100% with water, the amounts of the other components being as shown.

490 Alternatively, the unsubstituted chalcone can be replaced with an equivalent quantity of another flavonoid (e.g., another chalcone, flavanone, isoflavone, coumarin, flavone, chromone, dicoumarol, chromanone, chromanol, or mixtures thereof).

495 While particular embodiments of the subject invention have been described, it will be obvious to those skilled in the art that various changes and modifications to the subject invention can be made without departing from the spirit and scope of the invention. It is intended to cover, in the appended claims, all such modifications that are within the scope of the subject invention.

## WHAT IS CLAIMED IS:

1. A method of regulating the visible and/or tactile discontinuities in the texture of mammalian skin, comprising applying to skin in need of such treatment a safe and effective amount of a skin care composition comprising:
  - 5 (a) a safe and effective amount of a skin texture regulating agent consisting essentially of flavonoids selected from the group consisting of:
    - (i) flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof;
    - (ii) chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof;
    - 10 (iii) flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof;
    - (iv) one or more isoflavones;
    - (v) coumarins selected from the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof;
    - 15 (vi) chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures thereof;
    - (vii) one or more dicoumarols;
    - (viii) one or more chromanones;
  - 20 (ix) one or more chromanol; and
  - (x) mixtures thereof;
- and
- (b) a dermatologically acceptable carrier for the skin texture regulating agent.

30 2. A method for reducing post-inflammatory hyperpigmentation in mammalian skin, comprising applying to skin in need of such treatment a safe and effective amount of a skin care composition comprising:

35 (a) a safe and effective amount of a skin post-inflammatory hyperpigmentation reducing agent consisting essentially of flavonoids selected from the group consisting of:

(i) flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof;

(ii) chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof;

40 (iii) flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof;

(iv) one or more isoflavones;

45 (v) coumarins selected from the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof;

(vi) chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures thereof;

50 (vii) one or more dicoumarols;

(viii) one or more chromanones;

(ix) one or more chromanol; and

(x) mixtures thereof;

55 and

(b) a dermatologically acceptable carrier for the skin post-inflammatory hyperpigmentation reducing agent.

60 3. A method for reducing the non-melanin discoloration of mammalian skin, comprising applying to skin in need of such treatment a safe and effective amount of a skin care composition comprising:

- (a) a safe and effective amount of a skin non-melanin discoloration reducing agent consisting essentially of flavonoids selected from the group consisting of:
- (i) flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof;
- (ii) chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof;
- (iii) flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof;
- (iv) one or more isoflavones;
- (v) coumarins selected from the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof;
- (vi) chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures thereof;
- (vii) one or more dicoumarols;
- (viii) one or more chromanones;
- (ix) one or more chromanol; and
- (x) mixtures thereof;
- and
- (b) a dermatologically acceptable carrier for the non-melanin discoloration regulating agent.
4. A method for regulating the moisturization and barrier properties of mammalian skin, comprising applying to skin in need of such treatment a safe and effective amount of a skin care composition comprising:
- (a) a safe and effective amount of a skin moisturizing agent consisting essentially of flavonoids selected from the group consisting of:

- (i) flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof;
- (ii) chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof;
- 95 (iii) flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof;
- (iv) one or more isoflavones;
- 100 (v) coumarins selected from the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof;
- (vi) chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures thereof;
- 105 (vii) one or more dicoumarols;
- (viii) one or more chromanones;
- (ix) one or more chromanol; and
- (x) mixtures thereof;
- 110 and
- (b) a dermatologically acceptable carrier for the skin moisturizing agent.
5. A method for regulating the epidermal differentiation of mammalian skin, comprising applying to skin in need of such treatment a safe and effective amount of a skin care composition comprising:
- 115 (a) a safe and effective amount of epidermal differentiation regulating agent consisting essentially of flavonoids selected from the group consisting of:
- (i) flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof;

- 120 (ii) chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof;

125 (iii) flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof;

(iv) one or more isoflavones;

(v) coumarins selected from the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof;

130 (vi) chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures thereof;

(vii) one or more dicoumarols;

(viii) one or more chromanones;

135 (ix) one or more chromanol; and

(x) mixtures thereof;

and

(b) a dermatologically acceptable carrier for the epidermal differentiation regulating agent.

140 6. A method for regulating exfoliation of mammalian skin, comprising applying to skin in need of such treatment a safe and effective amount of a skin care composition comprising:

145 (a) a safe and effective amount of a skin exfoliation regulating agent consisting essentially of flavonoids selected from the group consisting of:

(i) flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof;

(ii) chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof;

- (iii) flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof;
- (iv) one or more isoflavones;
- 155 (v) coumarins selected from the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof;
- (vi) chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures thereof;
- 160 (vii) one or more dicoumarols;
- (viii) one or more chromanones;
- (ix) one or more chromanol; and
- (x) mixtures thereof,
- 165 and
- (b) a dermatologically acceptable carrier for the exfoliation regulating agent.
7. A method for thickening of skin to reduce skin atrophy, comprising applying to skin in need of such treatment a safe and effective amount of a skin care composition comprising:
- 170 (a) a safe and effective amount of a skin thickening agent consisting essentially of flavonoids selected from the group consisting of:
- (i) flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof;
- 175 (ii) chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof;
- (iii) flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof;
- 180 (iv) one or more isoflavones;

- (v) coumarins selected from the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof;
- (vi) chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures thereof;
- (vii) one or more dicoumarols;
- (viii) one or more chromanones;
- (ix) one or more chromanol; and
- (x) mixtures thereof;

and

- (b) a dermatologically acceptable carrier for the skin thickening agent.

8. A method for regulating the elasticity of mammalian skin, comprising applying to skin in need of such treatment a safe and effective amount of a skin care composition comprising:
- (a) a safe and effective amount of a skin elasticity regulating agent consisting essentially of flavonoids selected from the group consisting of:
- (i) flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof;
- (ii) chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof;
- (iii) flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof;
- (iv) one or more isoflavones;
- (v) coumarins selected from the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof;

- (vi) chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures thereof;
- 215 (vii) one or more dicoumarols;
- (viii) one or more chromanones;
- (ix) one or more chromanol; and
- (x) mixtures thereof;
- and
- 220 (b) a dermatologically acceptable carrier for the skin elasticity regulating agent.
9. A method for reducing oily skin, comprising applying to mammalian skin in need of such treatment a safe and effective amount of a skin care composition comprising:
- 225 (a) a safe and effective amount of a skin oil reducing agent consisting essentially of flavonoids selected from the group consisting of:
- (i) flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof;
- (ii) chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof;
- 230 (iii) flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof;
- (iv) one or more isoflavones;
- (v) coumarins selected form the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof;
- (vi) chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures thereof;
- 240 (vii) one or more dicoumarols;

- (viii) one or more chromanones;
- (ix) one or more chromanol; and
- (x) mixtures thereof,
- and
- (b) a dermatologically acceptable carrier for the skin oil reducing agent.
10. A method for regulating cellulite in mammalian skin, comprising applying to  
skin in need of such treatment a safe and effective amount of a skin care  
composition comprising:
- (a) a safe and effective amount of a skin cellulite reducing agent consisting  
essentially of flavonoids selected from the group consisting of:
- (i) flavanones selected from the group consisting of unsubstituted  
flavanones, mono-substituted flavanones, and mixtures thereof;
- (ii) chalcones selected from the group consisting of unsubstituted  
chalcones, mono-substituted chalcones, di-substituted chalcones,  
tri-substituted chalcones, and mixtures thereof;
- (iii) flavones selected from the group consisting of unsubstituted  
flavones, mono-substituted flavones, di-substituted flavones, and  
mixtures thereof;
- (iv) one or more isoflavones;
- (v) coumarins selected form the group consisting of unsubstituted  
coumarins, mono-substituted coumarins, di-substituted coumarins,  
and mixtures thereof;
- (vi) chromones selected from the group consisting of unsubstituted  
chromones, mono-substituted chromones, di-substituted  
chromones, and mixtures thereof;
- (vii) one or more dicoumarols;
- (viii) one or more chromanones;
- (ix) one or more chromanol; and
- (x) mixtures thereof;
- and

- (b) a dermatologically acceptable carrier for the skin cellulite reducing agent.
- 275 11. A method for reducing pruritus in mammalian skin, comprising applying to skin in need of such treatment a safe and effective amount of a skin care composition comprising:
- (a) a safe and effective amount of a pruritus reducing agent consisting essentially of flavonoids selected from the group consisting of:
- 280 (i) flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof;
- (ii) chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof;
- 285 (iii) flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof;
- (iv) one or more isoflavones;
- (v) coumarins selected from the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof;
- 290 (vi) chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures thereof;
- 295 (vii) one or more dicoumarols;
- (viii) one or more chromanones;
- (ix) one or more chromanols; and
- (x) mixtures thereof;
- and
- 300 (b) a dermatologically acceptable carrier for the pruritus reducing agent.

12. A method for promoting wound healing in mammalian skin, comprising applying to skin in need of such treatment a safe and effective amount of a skin care composition comprising:

- (a) a safe and effective amount of a skin wound healing promoting agent consisting essentially of flavonoids selected from the group consisting of:
- (i) flavanones selected from the group consisting of unsubstituted flavanones, mono-substituted flavanones, and mixtures thereof;
- (ii) chalcones selected from the group consisting of unsubstituted chalcones, mono-substituted chalcones, di-substituted chalcones, tri-substituted chalcones, and mixtures thereof;
- (iii) flavones selected from the group consisting of unsubstituted flavones, mono-substituted flavones, di-substituted flavones, and mixtures thereof;
- (iv) one or more isoflavones;
- (v) coumarins selected from the group consisting of unsubstituted coumarins, mono-substituted coumarins, di-substituted coumarins, and mixtures thereof;
- (vi) chromones selected from the group consisting of unsubstituted chromones, mono-substituted chromones, di-substituted chromones, and mixtures thereof;
- (vii) one or more dicoumarols;
- (viii) one or more chromanones;
- (ix) one or more chromanol; and
- (x) mixtures thereof;
- and
- (b) a dermatologically acceptable carrier for the skin wound healing promoting agent.